In any representation of the primary pathways responsible for the processing of sensory stimuli or motor inputs, it is notable that monoaminergic (noradrenergic, serotonergic, dopaminergic) neurons do not appear to be involved. The anatomical divergence of these latter neurons suggests that their networks are superimposed on those conveying sensory or motor signals. We have found some evidence that monoaminergic neurons, especially dopaminergic ones, favor the functional role of one or another cerebral structure, depending on the behavioural and external situations the animal is exposed to. These results seem important since dopaminergic neurons are extremely sensitive to most of the pharmacological products which induce addiction.

Amphetamine and cocaine increase the quantities of dopamine in the synaptic cleft. Moreover, dopaminergic neurons which innervate cortical and subcortical structures possess nicotinic receptors and are regulated by small interneurons which bear μ-opioid receptors. We have shown that repeated exposure to morphine increases the activity of dopaminergic neurons innervating *subcortical* structures. At the opposite, animals repeatedly exposed to nicotine demonstrate an activation of dopaminergic neurons innervating *cortical* structures, whereas dopaminergic neurons innervating *subcortical* structures remain unaffected.

Given that drug abuse necessarily involves repeated exposure to the drug and that such exposure to the nicotine was found to reduce its stimulatory effect on subcortical neurons, these results suggest that nicotine differs importantly from other abused drugs such as opiates and psychomotor stimulants. These latter are indeed generally accepted to achieve their rewarding properties through the activation of subcortical dopaminergic neurons.

Our data indicate that, in addition to subcortical structures such as the nucleus accumbens, prefrontal cortex may be a site involved in drug reward. Since dopaminergic neurons innervating cortical structures play a major role in cognitive processes, it can be proposed, therefore, that the activation of these neurons by nicotine represents the physiological basis of tobacco smoking's facilitatory effects on learning and increased attention. Such effects may be an important basis for the pursuit of nicotine.

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2023251863

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